

Attorney Docket No. A-65686-1/463037-17/RMS/RMK/JML

PATENT

1634  
#2010  
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10/15/02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

RECEIVED

In re application of:

Examiner: FRANK MEI MIN LU

DUONG, et al.

Group Art Unit: 1634

Serial No.: 09/397,957

CERTIFICATE OF MAILING

TECH CENTER 1600/2900

Filing Date: 17 SEPTEMBER 1999

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For: **SIGNAL DETECTION TECHNIQUES  
FOR THE DETECTION OF ANALYTES**

Signed

Mary McFarland  
Mary McFarland

RESPONSE TO RESTRICTION REQUIREMENT AND AMENDMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Following is Applicants' response to the Restriction Requirement mailed 27 August 2002. A response is due 27 September 2002, making this a timely response. Please amend the application as follows:

IN THE CLAIMS

Please withdraw claims 15, 20, 31-34, 41-42, 49 and 50 from consideration until such time as a generic claim is found allowable.

Please amend claim 39 to read as follows:

39. (Amended) The method of claim 11, wherein said input waveform is a voltage waveform comprising a square wave.

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**REMARKS**

Claims 11, 14, 19, 28-30, 35-40, and 43-48 are pending in this application. Claims 15, 20, 31-34, 41-42, 49, and 50 have been withdrawn from consideration. Claim 39 is amended herein. Support for the amendment to claim 39 can be found at least in originally filed claim 36. A marked-up version of paragraphs and claims amended as above is attached herein, entitled **Version with Markings to Show Changes Made**. For the Examiner's convenience, a clean copy of all pending claims is attached, entitled **"Appendix A: Pending Claims"**.

**Elections**

The Examiner stated that Applicants are required under 35 U.S.C. §121 to elect a single disclosed species among:

1. nucleic acid (claim 14); and
2. protein (claim 15)

Applicants hereby elect Species 1, nucleic acid, claim 14, without traverse. Applicants note that the claims will be restricted to this species if no generic claim is held allowable. Accordingly, Applicants have withdrawn Claim 15 from consideration until such time as a generic claim may be found allowable, with claims 11, 19, 20, and 28-50 being generic.

The Examiner further required Applicants under 35 U.S.C. §121 to elect a single disclosed species among:

1. the use of a peak recognition scheme (claim 19); and
2. a digital filter (claims 20, 49, and 50)

Applicants hereby elect the use of a peak recognition scheme (claim 19), without traverse. Applicants note that the claims will be restricted to this species if no generic claim is held allowable. Accordingly, Applicants have withdrawn Claims 20, 49 and 50 from consideration until such time as a generic claim may be found allowable, with claims 11, 14, 15, and 28-48 being generic.

The Examiner still further required Applicants under 35 U.S.C. §121 to elect a single disclosed species among:

1. ferrocyanide (claim 32); and
2. a lower redox potential than an electron transfer moiety (claim 33).

Applicants hereby elect ferrocyanide, claim 32, without traverse. Applicants note that the claims will be restricted to this species if no generic claim is held allowable. Accordingly, Applicants have withdrawn Claim 33 from consideration until such time as a generic claim may be found allowable, with claims 11, 14, 15, 19, 20, 28-31, and 34-50 being generic.

The Examiner yet further required Applicants under 35 U.S.C. §121 to elect a single disclosed species among:

1. further comprising adding a co-reductant to said sample (claims 31-33)
2. further comprising adding a co-oxidant to said sample (claim 34)
3. further comprising computing a fast fourier transform of said detected output waveform (claim 41)
4. further comprising computing a joint time frequency transform of said detected output waveform (claim 42); and
5. further comprising fitting said harmonic components to a first curve and a second curve (claims 44-48)

Applicants hereby elect Species 5, further comprising fitting said harmonic components to a first curve and a second curve, claims 44-48, without traverse. Applicants note that the claims will be restricted to this species if no generic claim is held allowable. Accordingly, Applicants have withdrawn claims 31-34, and claims 41-42 from consideration until such time as a generic claim may be found allowable, with claims 11, 14, 15, 19, 20, 28-30, 35-40, 43, 49, and 50 being generic.

The Examiner still yet further required Applicants under 35 U.S.C. §121 to elect a single disclosed species among:

1. a voltage wave (claim 36); and
2. a square wave (claim 39)

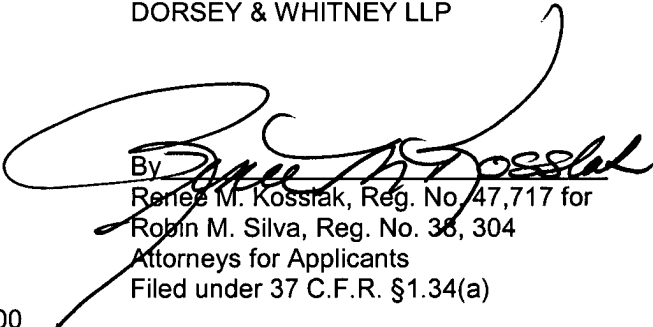
Applicants hereby elect a voltage wave (claim 36), without traverse and note that the claims may be restricted to this species if no generic claim is held allowable.

However, Applicants have amended claim 39 to recite 'wherein said input waveform is a voltage waveform comprising a square wave'. Applicants submit that both claims 36 and amended claim 39 read on Species 1, and respectfully request that both claims be examined even if no generic claim is held allowable (with claims 11, 14, 15, 18, 19, 28-35, 37, 38, and 40-50 being generic).

## CONCLUSION

Applicants submit the claims are in condition for allowance, and notification of such is respectfully requested. If after review, the Examiner feels there are further unresolved issues, the Examiner is invited to call the undersigned at (415) 781-1989. Enclosed is our check to cover the cost of added claims not already paid for. While Applicant believes that no further fees are due at this time, the Commissioner is authorized to charge any fees that may be due as a result of filing this amendment, including additional claims fees not already paid for, or other fees that have not been separately paid, to Deposit Account 50-2319 (Order No. 463037-00017 [A-65686-1/RMS/RMK/JML]).

Respectfully submitted,  
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## APPENDIX WITH MARKINGS SHOWING CHANGES MADE

Claim 39 was amended as follows:

39. (Amended) The method of claim 11, wherein said input waveform is a voltage waveform comprisinging a square wave.

Claims 15, 20, 31-34, 41-42, 49 and 50 were withdrawn from consideration.

## **Appendix A: Pending Claims**

11. A method of determining the presence of target analytes in a sample comprising:
- a) applying said sample to an array comprising a plurality of electrodes, at least one of which comprises an assay complex comprising:
    - i) a capture binding ligand covalently attached to said electrode;
    - ii) a target analyte; and
    - iii) an electron transfer moiety;
  - b) applying an input waveform to said electrode to generate an output waveform comprising a harmonic component;
  - c) detecting said output waveform at said electrode;
  - d) analyzing said harmonic component to determine the presence of said target analytes.
14. A method according to claim 11 wherein said target analyte is a nucleic acid.
19. A method according to claim 11, wherein said analyzing comprises the use of a peak recognition scheme.
28. The method of claim 11, wherein said electrode has an asymmetrical response to said input waveform.
29. The method of claim 28, wherein said electron transfer moiety is degradable.
30. The method of claim 29, wherein said electron transfer moiety is luminol.
35. The method of claim 28, wherein said asymmetrical response is due to an enzyme-coupled reaction.
36. The method of claim 11, wherein said input waveform is a voltage waveform and said output waveform is a current waveform, wherein said input waveform comprises an AC component having a first frequency and a first amplitude, and wherein said first amplitude is selected such that said output waveform comprises at least one non-linear harmonic component.
37. The method of claim 11, wherein said harmonic component is chosen from the group consisting of the second, third, fourth, fifth, sixth, seventh, eighth, ninth, and tenth harmonic components.
38. The method of claim 11, wherein said method comprises analyzing a plurality of harmonic components of said output waveform.

39. (Amended) The method of claim 11, wherein said input waveform is a voltage waveform comprising a square wave.

40. The method of claim 39, wherein said harmonic component is an even harmonic component.

43. The method of claim 11, wherein said input waveform comprises a plurality of components, each having a different frequency.

44. The method of claim 11, further comprising fitting said harmonic component to a first curve and a second curve, wherein said first curve describes a Faradaic signal and said second curve describes a background signal.

45. The method of claim 44, wherein said first curve is based, at least in part, on a modified Gaussian distribution.

46. The method of claim 44, wherein said second curve is a fifth order polynomial.

47. The method of claim 44, wherein said fitting comprises minimizing a mean square error.

48. The method of claim 46, wherein said fitting said fifth order polynomial comprises using singular value decomposition.